

1. (Once Amended) A transgenic non-human mammal comprising a transgene comprising a mutant GP IIIa gene wherein said mutant gene encodes a mutant GPIIIa protein, said mutant protein having one or more phosphorylatable cytoplasmic domain tyrosine residues replaced with a non-tyrosine residue.

2. (Once Amended) The transgenic non-human mammal of claim 1 wherein said non-tyrosine residue is phenylalanine.

3. (Once Amended) The transgenic non-human mammal of claim 1 wherein said phosphorylatable cytoplasmic domain tyrosine residues are tyrosine residues 747 and 759 of SEQ ID No 1.

4. (Once Amended) Platelets isolated from the blood plasma of said transgenic non-human mammal of claim 1.

5. (Once Amended) The transgenic non-human mammal of claim 1 wherein said transgenic non-human mammal is selected from the group consisting of sheep, goat, mouse, pig, dog, cat, monkey, chimpanzee, hamster, rat, rabbit, cow and guinea pig.

6. (Once Amended) The transgenic non-human mammal of claim 5 wherein said non-human mammal is a mouse.

7. (Once Amended) The transgenic non-human mammal of claim 1 wherein two phosphorylatable cytoplasmic domain tyrosine residues have been replaced with a non-tyrosine residue.

8. (Once Amended) The transgenic non-human mammal of claim 7 wherein said non-tyrosine residues are phenylalanine.

9. (Once Amended) The transgenic non-human mammal of claim 7 wherein said phosphorylatable cytoplasmic domain tyrosine residues are tyrosine residues 747 and 759 of SEQ ID No 1.

10. (Once Amended) Platelets isolated from blood plasma of said transgenic [the] non-human mammal of claim 7.

25 11. (Once Amended) The transgenic non-human mammal of claim 7 wherein said transgenic non-human mammal is selected from the group consisting of sheep, goat, mouse, pig, dog, cat, monkey, chimpanzee, hamster, rat, rabbit, cow and guinea pig.

12. (Once Amended) The transgenic non-human mammal of claim 11 wherein said transgenic non-human mammal is a mouse.

13. (Once Amended) A transgenic non-human mammal expressing a transgene integrated into its genome, wherein said transgene comprises DNA encoding mutant GP IIIa protein, wherein one or more phosphorylatable cytoplasmic domain tyrosine residues has been replaced with a non-tyrosine residue.

14. (Once Amended) The transgenic non-human mammal of claim 13 wherein said non-tyrosine residue is phenylalanine.

15. (Once Amended) The transgenic non-human mammal of claim 13 wherein said phosphorylatable cytoplasmic domain tyrosine residues are tyrosine residues 747 and 759 of SEQ ID No. 1.

16. (Once Amended) Platelets isolated from blood plasma of said transgenic non-human mammal of claim 13.

17. (Once Amended) The transgenic non-human mammal of claim 13 wherein said transgenic non-human mammal is selected from the group consisting of sheep, goat, mouse, pig, dog, cat, monkey, chimpanzee, hamster, rat, rabbit, cow and guinea pig.

18. (Once Amended) The transgenic non-human mammal of claim 17 wherein said transgenic non-human mammal is a mouse.

Q<sup>5</sup> 19. (Once Amended) The transgenic non-human mammal of claim 13 wherein two phosphorylatable cytoplasmic domain tyrosine residues have been replaced with a non-tyrosine residue.

20. (Once Amended) The transgenic non-human mammal of claim 19 wherein said non-tyrosine residue is phenylalanine.

21. (Once Amended) The transgenic non-human mammal of claim 19 wherein said phosphorylatable cytoplasmic domain tyrosine residues are tyrosine residues 747 and 759 of SEQ ID No. 1.

22. (Once Amended) Platelets isolated from blood plasma of said transgenic non-human mammal of claim 19.

23. (Once Amended) The transgenic non-human mammal of claim 19 wherein said transgenic non-human mammal is selected from the group consisting of sheep, goat, mouse, pig, dog, cat, monkey, chimpanzee, hamster, rat, rabbit, cow and guinea pig.

24. (Once Amended) The transgenic non-human mammal of claim 23 wherein said transgenic non-human mammal is a mouse.

25. (Once Amended) A method of preparing a transgenic non-human mammal comprising a transgene comprising a mutant GP IIIa gene, wherein said mutant gene encodes a mutant GP IIIa protein, said mutant protein having one or more cytoplasmic domain tyrosine residues replaced with a non-tyrosine residue, said method comprising:

- a) introducing into embryonic stem cells a nucleic acid molecule comprising said transgene comprising said mutant GP IIIa gene, wherein said mutant gene encodes said mutant GP IIIa protein;
- b) generating a transgenic non-human mammal from the cells of step a).

26. (Once Amended) The method of claim 25 wherein said non-tyrosine residue is phenylalanine.

27. (Once Amended) The method of claim 25 wherein said phosphorylatable cytoplasmic domain tyrosine residues are tyrosine residues 747 and 759 of SEQ ID No. 1.

28. (Once Amended) The method of claim 25 wherein said transgenic non-human mammal is selected from the group consisting of sheep, goat, mouse, pig, dog, cat, monkey, chimpanzee, hamster, rat, rabbit, cow and guinea pig.

29. (Once Amended) The method of claim 28 wherein said transgenic non-human mammal is a mouse.

30. (Once Amended) The method of claim 25 wherein two or more phosphorylatable cytoplasmic domain tyrosine residues have been replaced with a non-tyrosine residue.

31. (Once Amended) The method of claim 30 wherein said non-tyrosine residues are phenylalanine.

32. (Once Amended) The method of claim 30 wherein said phosphorylatable cytoplasmic domain tyrosine residues are tyrosine residues 747 and 759 of SEQ ID No. 1.

33. (Once Amended) The method of claim 30 wherein said transgenic non-human mammal is selected from the group consisting of sheep, goat, mouse, pig, dog, cat, monkey, chimpanzee, hamster, rat, rabbit, cow and guinea pig.

34. (Once Amended) The method of claim 33 wherein said transgenic non-human mammal is a mouse.

35. (Once Amended) The method of claim 25 further comprising mating said transgenic non-human mammal, followed by selecting a non-human mammal homozygous for said mutant GP IIIa gene.

36. (Once Amended) The method of claim 35 wherein said transgenic non-human mammal is a mouse.

37. (Once Amended) A method of preparing a transgenic non-human mammal comprising a transgene comprising a mutant GP IIIa gene encoding a mutant GP IIIa protein, said mutant protein having one or more phosphorylatable cytoplasmic domain tyrosine residues replaced with a non-tyrosine residue, said method comprising:

- a) introducing into embryonic stem cells a nucleic acid molecule comprising a transgene comprising said mutant GP IIIa gene encoding mutant GP IIIa

- protein and a selectable marker flanked by FRT sites, to produce one or more transformed embryonic stem cells;
- b) identifying and selecting said transformed cells;
  - c) removing said selectable marker from said transformed cells selected in step b) by transient transformation with FLP recombinase;
  - d) injecting transformed cells from step c) into one or more blastocysts; and,
  - e) generating a transgenic non-human mammal from said blastocysts of step d), wherein said transgenic non-human mammal comprising said transgene comprising mutant GP IIIa gene is heterozygous for said mutant GP IIIa gene.

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38. (Once Amended) The method of claim 37 wherein said non-tyrosine residue is phenylalanine.

39. (Once Amended) The method of claim 37 wherein said phosphorylatable cytoplasmic domain tyrosine residues are tyrosine residues 747 and 759 of SEQ ID No. 1.

40. (Once Amended) The method of claim 37 wherein said transgenic non-human mammal is selected from the group consisting of sheep, goat, mouse, pig, dog, cat, monkey, chimpanzee, hamster, rat, rabbit, cow and guinea pig.

41. (Once Amended) The method of claim 37 wherein said transgenic non-human mammal is a mouse.

42. (Once Amended) The method of claim 37 wherein two phosphorylatable cytoplasmic domain tyrosine residues have been replaced with a non-tyrosine residue.

43. (Once Amended) The method of claim 37 wherein said non-tyrosine residues are phenylalanine.

44. (Once Amended) The method of claim 37 wherein said phosphorylatable cytoplasmic domain tyrosine residues are tyrosine residues 747 and 759 of SEQ ID No. 1.

45. (Once Amended) The method of claim 43 wherein said transgenic non-human mammal is selected from the group consisting of sheep, goat, mouse, pig, dog, cat, monkey, chimpanzee, hamster, rat, rabbit, cow and guinea pig.

46. (Once Amended) The method of claim 45 wherein said transgenic non-human mammal is a mouse.

47. (Once Amended) The method of claim 37 further comprising mating said transgenic non-human mammal, followed by selecting a transgenic non-human mammal homozygous for said mutant GP IIIa gene.

48. (Once Amended) The method of claim 47 wherein said non-human mammal is a mouse.

49. (Once Amended) The method of claim 37 further comprising:

- f) mating a heterozygous transgenic non-human mammal with a second heterozygous transgenic non-human mammal; and,
- h) selecting a transgenic non-human mammal homozygous for the mutant GP IIIa gene from the resulting progeny.

50. (Once Amended) The method of claim 49 wherein said transgenic non-human mammal is a mouse.

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51. (Once Amended) A method for determining mutant GP IIIa protein modulation of one or more biological responses, said method comprising:

treating transgenic and non-transgenic non-human mammals with one or more agents affecting said one or more biological responses; and,

comparing said one or more biological responses between a transgenic and a non-transgenic non-human mammal of the same species, wherein said non-transgenic non-human mammal comprises wild-type GP IIIa genes and the transgenic, non-human mammal comprises one or more mutant GP IIIa genes, wherein said mutant gene encodes a mutant GP IIIa protein, said mutant protein having at least one or more phosphorylatable cytoplasmic domain tyrosine residues replaced with a non-tyrosine residue in the mutant GP IIIa gene.

52. (Once Amended) The method of claim 51 wherein said non-tyrosine residue is phenylalanine.

53. (Once Amended) The method of claim 51 wherein said phosphorylatable cytoplasmic domain tyrosine residues are tyrosine residues 747 and 759 of SEQ ID No. 1.

54. (Once Amended) The method of claim 51 wherein said transgenic and non-transgenic non-human mammals are selected from the group consisting of sheep, goat, mouse, pig, dog, cat, monkey, chimpanzee, hamster, rat, rabbit, cow and guinea pig.

55. (Once Amended) The method of claim 54 wherein said non-human mammal is a mouse.

56. (Once Amended) The method of claim 51 wherein two phosphorylatable cytoplasmic domain tyrosine residues have been replaced with a non-tyrosine residue.



57. (Once Amended) The method of claim 56 wherein said non-tyrosine residues are phenylalanine.

58. (Once Amended) The method of claim 56 wherei said phosphorylatable cytoplasmic domain tyrosine residues are tyrosine residues 747 and 759 of SEQ ID NO. 1.

59. (Once Amended) The method of claim 56 wherein said transgenic and non-transgenic non-human mammals are selected from the group consisting of sheep, goat, mouse, pig, dog, cat, monkey, chimpanzee, hamster, rat, rabbit, cow and guinea pig.

60. (Once Amended) The method of claim 59 wherein said transgenic non-human mammal is a mouse.

61. (Once Amended) The method of claim 51 wherein said biological response is bleeding time.

62. (Once Amended) The method of claim 51 wherein said biological response is thrombotic response.

63. (Once Amended) The method of claim 51 wherein said biological response is angiogenesis.

64. (Once Amended) The method of claim 5 wherein said biological response is tumor metastasis.

65. (Once Amended) The method of claim 5 wherein said biological response is inflammation.

66. (Once Amended) The method of claim 51 wherein said mammal is a mouse.

67. (Once Amended) A method of determining the effect of an agent on a biological response of a transgenic, non-human mammal wherein said biological response is modulated by GP IIIa phosphorylation, said method comprising:

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- a) administering said agent to said transgenic non-human mammal of claim 1;
  - b) maintaining said transgenic, non-human mammal for a desired period of time after administering said agent; and,
  - c) determining the effect of said agent on a biological response modulated by mutant GP IIIa phosphorylation in said transgenic, non-human mammal.

68. (Once Amended) The method of claim 67 wherein said transgenic, non-human mammal is a mouse.

Please insert the following page into the specification following the claims.